STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 142502

TO: Rei-Tsang Shiao **Location: 5a10 / 5c18** **Saturday, January 15, 2005** **Art Unit: 1626** **Phone: 272-0707** **Serial Number: 10 / 816957**	**From: Jan Delaval** **Location: Biotech-Chem Library** **Rem 1a51** **Phone: 272-2504** **jan.delaval@uspto.gov**

Search Notes

sira
Search and Information Resources Administration

Access DB# 142502

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Robert (Rob) Shin Examiner #: 7952 Date: 1/13/05
Art Unit: 1626 Phone Number 30 2-0909 Serial Number: 10/816,957
Mail Box and Bldg/Room Location: 5A10/5C18 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

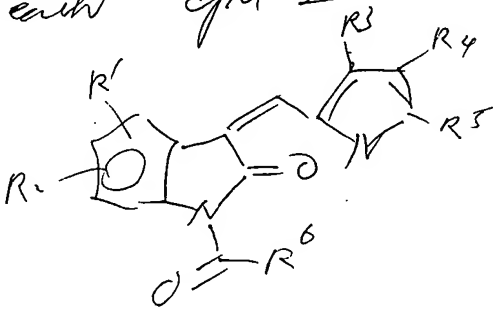
Title of Invention: Binding of a 3-(pyrrole)

Inventors (please provide full names): Saqef al

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

I. Search cpd I



* R' ~ R6 are sub

II method of use of cpd I

****

STAFF USE ONLY		Type of Search		Vendors and cost where applicable	
Searcher:	Jan	NA Sequence (#)		STN	✓
Searcher Phone #:	22504	AA Sequence (#)		Dialog	
Searcher Location:		Structure (#)	✓	Questel/Orbit	
Date Searcher Picked Up:	1/15/05	Bibliographic		Dr.Link	
Date Completed:	1/15/05	Litigation		Lexis/Nexis	
Searcher Prep & Review Time:		Fulltext		Sequence Systems	
Clerical Prep Time:	15	Patent Family		WWW/Internet	
Online Time:	+ 20	Other		Other (specify)	

PTO-1590 (8-01)

=> fil reg
FILE 'REGISTRY' ENTERED AT 10:28:16 ON 15 JAN 2005

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 12 JAN 2005 HIGHEST RN 812631-13-3
DICTIONARY FILE UPDATES: 12 JAN 2005 HIGHEST RN 812631-13-3

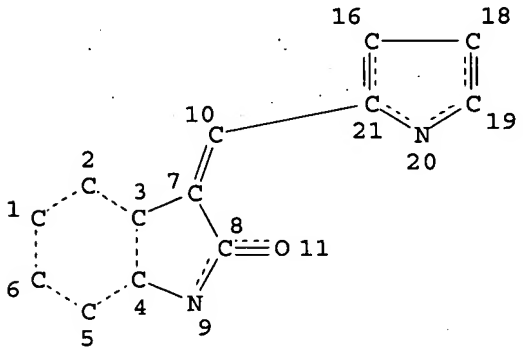
TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

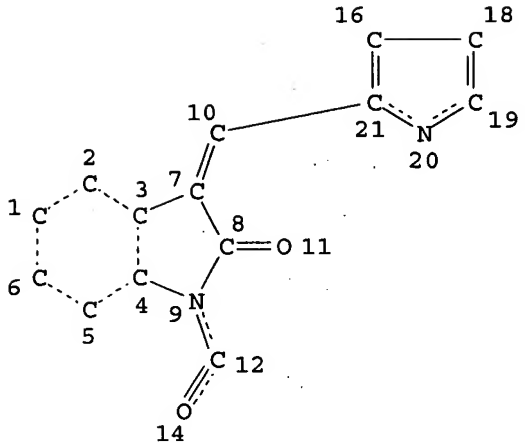
=> d sta que l28
L20 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

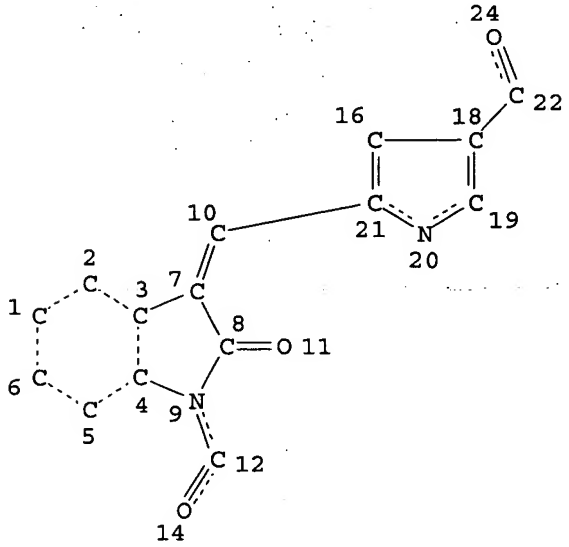
STEREO ATTRIBUTES: NONE
L22 2680 SEA FILE=REGISTRY SSS FUL L20
L23 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
L25 48 SEA FILE=REGISTRY SUB=L22 SSS FUL L23
L26 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
L28 0 SEA FILE=REGISTRY SUB=L25 SSS FUL L26

100.0% PROCESSED 0 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

=> => fil marpat
FILE 'MARPAT' ENTERED AT 10:31:10 ON 15 JAN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

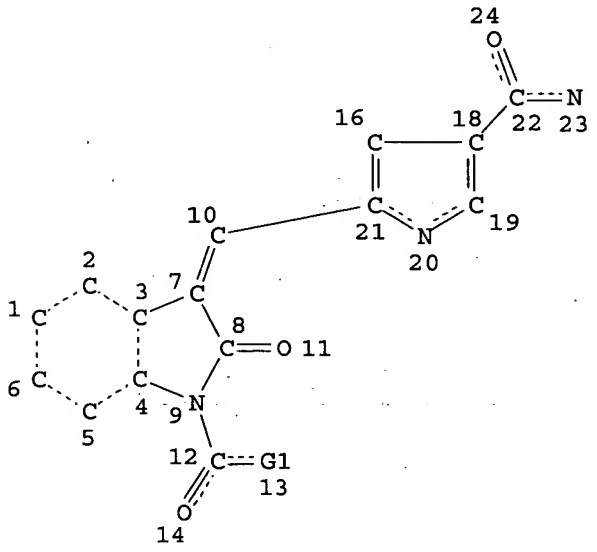
FILE CONTENT: 1988-PRESENT (VOL 142 ISS 01)(20050107/ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 6806291 19 OCT 2004
DE 10316402 21 OCT 2004
EP 1471568 27 OCT 2004
JP 2004300045 14 NOV 2004
WO 2004101522 25 NOV 2004

Structure search limits have been raised. See HELP SLIMIT for the new, higher limits.

=> d sta que
L15 STR

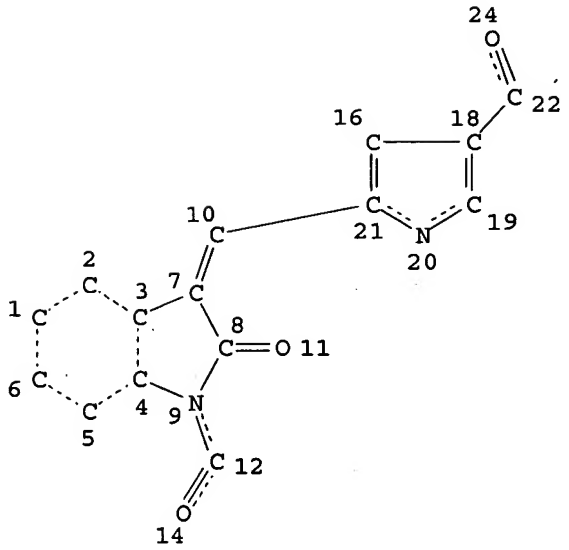


N @15

VAR G1=O/15
NODE ATTRIBUTES:
NSPEC IS RC AT 15
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE
L26 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
L30 8 SEA FILE=MARPAT SSS FUL L26
L31 4 SEA FILE=MARPAT SUB=L30 SSS FUL L15

100.0% PROCESSED 8 ITERATIONS 4 ANSWERS
SEARCH TIME: 00.00.01

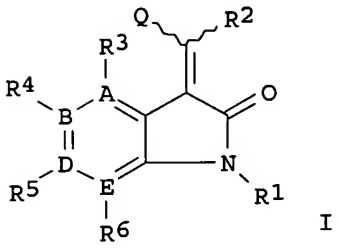
=> => d bib abs qhit retable tot l31

L31 ANSWER 1 OF 4 MARPAT COPYRIGHT 2005 ACS on STN
AN 138:4517 MARPAT
TI Preparation of 3-heteroarylmethylidene-2-indolinone protein kinase inhibitors for use against cancer and other disorders
IN McMahon, Gerald; Tang, Peng Cho; Sun, Li
PA Sugen, Inc., USA
SO U.S., 64 pp., Cont.-in-part of U.S. Ser. No. 74,621.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

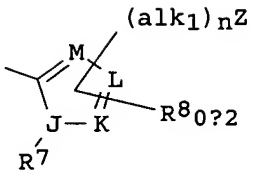
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6486185	B1	20021126	US 1998-191458	19981112
	US 6316429	B1	20011113	US 1998-74621	19980507
	US 2002156083	A1	20021024	US 2001-819698	20010329
	US 6683082	B2	20040127		
	US 2004106630	A1	20040603	US 2003-725079	20031202
	US 2004106618	A1	20040603	US 2003-725267	20031202
PRAI	US 1997-45838P	19970507			
	US 1997-59677P	19970919			
	US 1998-74621	19980507			

US 2001-819698 20010329

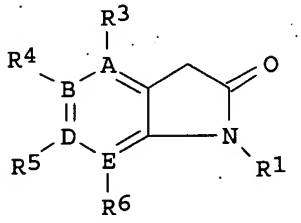
GI



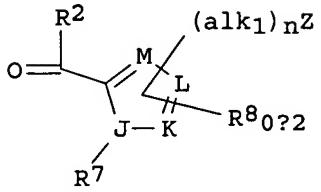
I



II



III

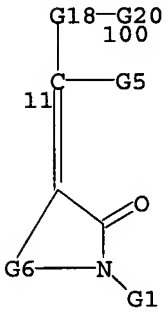


IV

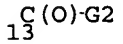
AB The present invention relates to novel 3-heteroarylidene-2-indolinone compds. (shown as I; e.g. 3-[3-(2-carboxyethyl)-4-methylpyrrol-2-methylidene]-2-indolinone) and physiol. acceptable salts thereof which modulate the activity of protein kinases and therefore are expected to be useful in the prevention and treatment of protein kinase related cellular disorders such as cancer. In I: A, B, D and E = C and N, it being understood that the N-containing 9-member bicyclic ring formed is one known in the chemical arts; it being further understood that when A, B, D, or E is N, R3, R4, R5 or R6, resp., does not exist. R1 = H, alkyl, cycloalkyl, aryl, hydroxy, alkoxy, carboxy, C-amido and sulfonyl; R2 = H, alkyl, cycloalkyl, aryl, heteroaryl, and heteroalicyclic; R3, R4, R5 and R6 = H, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, -SH, -S-alkyl, -S-cycloalkyl, -S-aryl, -S-heteroaryl, sulfinyl, sulfonyl, sulfonamido, carbonyl, carboxy, cyano, nitro, halo, -OC(O)NR10R11, N-carbamyl, -OC(S)NR10R11, N-thiocarbamyl, C-amido, N-amido, amino and -NR10R11; R10 and R11 = H, alkyl, cycloalkyl, aryl, carbonyl, sulfonyl and, combined, a five- or six-member heteroalicyclic ring containing at least one N; R3 and R4, R4 and R5, or R4 and R5 may combine to form a six-member aryl or heteroaryl ring. Q is a heteroaryl group II in which J = O, N and S; K, L and M = C, N, O and S such that the five-member heteroaryl ring formed is one known in the chemical arts, it being understood that when K, L and M are N, S or O, R8 or -(alk1)nZ cannot be covalently bonded to that atom; when J is N, R7 = H, alkyl, cycloalkyl, aryl, hydroxy, alkoxy, aryloxy, carbonyl, carboxy, C-amido, guanyl and sulfonyl and when J is O or S, R7 does not exist and there is no bond; R8 = H, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, -SH, -S-alkyl, -S-cycloalkyl, -S-aryl, -S-heteroaryl, sulfinyl, sulfonyl, sulfonamido, carbonyl, carboxy, cyano, nitro, halo, -OC(O)NR10R11, N-carbamyl, -OC(S)NR10R11, N-thiocarbamyl, C-amido, N-amido, amino, -NR10R11, trihalomethyl, a five member cycloalkyl, aryl, heteroaryl or heteroalicyclic ring fused to two adjacent atoms of the Q ring; and a six-member cycloalkyl, aryl, heteroaryl, or heteroalicyclic ring fused to two adjacent atoms of the Q ring. R10and R11 = H, alkyl, cycloalkyl, aryl, carbonyl, sulfonyl and, combined, a five- or six-member heteroalicyclic ring containing at least one N; alk1 = optionally substituted methylene (-CRR'-), optionally substituted ethylene (-C(R):C(R')-) and acetylene (-C.tplbond.C-); R and R' = H, alkyl, cycloalkyl, aryl, alkoxy,

-S-alkyl, -S-cycloalkyl, aryloxy and halo. N is 0 to 10, inclusive with the proviso that when n is 0, R7 is not alkyl substituted with aryl; and Z is a polar group hydroxy, alkoxy, carboxy, nitro, cyano, carbamyl, amino, quaternary ammonium, amido, ureido, sulfonamido, sulfinyl, sulfonyl, phosphono, phosphonyl, morpholino, piperazinyl and tetrazolo. Also claimed are a combinatorial library of ≥13 I and a method for synthesizing I comprising the step of reacting III with a 2nd reactant IV in a solvent and in the presence of a base at elevated temps. The IC50 results for 12 I for PDGFR, FLK-1R, EGFR, HER2 and IGF-1R protein tyrosine kinases (PTKs) are presented; IC50 refers to that amount of the tested compound needed to effect a 50% inhibition of PTK activity in the test indicated with respect to a control in which no compound of this invention is present. Thus, 3-(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-methylidenyl)-2-indolinone inhibited FLK-IR kinase with IC50 = 0.07 μM.

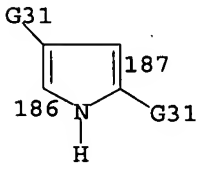
MSTR 1



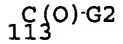
G1 = 13



G2 = OH / NH2
G6 = o-C6H4 (SO (1-) G7)
G18 = 186-11 187-100



G20 = 113



MPL: claim 1
NTE: or physiologically acceptable salts or prodrugs
NTE: substitution is restricted

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File

Akbasak	1992	111	119	J Neujrol Sci	CAPLUS
Akbasak	1992	111	119	J Neurol Sci	CAPLUS
Andreani	1998	48	727	Arzneimittel-Forschu	
Andreani	1998	48	727	Arzneimittel-Forschu	
Andreani	1997	32	919	Eur J Med Chem	CAPLUS
Andreani	1997	32	919	Eur J Med Chem	CAPLUS
Anon	1965			FR 1398224	CAPLUS
Anon	1988			EP 252713 A1	CAPLUS
Anon	1991			WO 9113055	CAPLUS
Anon	1991			WO 9115495	CAPLUS
Anon	1991			WO 9115495	CAPLUS
Anon	1992			WO 9207830	CAPLUS
Anon	1992			WO 9220642	CAPLUS
Anon	1992			WO 9220642	CAPLUS
Anon	1992			WO 9221660	CAPLUS
Anon	1992			WO 9231660	
Anon	1992			HU 923899	
Anon	1993			EP 0566226 A1	CAPLUS
Anon	1993			WO 9323040	CAPLUS
Anon	1994			WO 9403427	CAPLUS
Anon	1994			WO 9403427	CAPLUS
Anon	1994			WO 9410202	CAPLUS
Anon	1994			WO 9410202	CAPLUS
Anon	1994			WO 9414808	CAPLUS
Anon	1994			WO 9414808	CAPLUS
Anon	1995			WO 9514667	CAPLUS
Anon	1995			WO 9524190	CAPLUS
Anon	1996			WO 9600226	CAPLUS
Anon	1996			WO 9616964	CAPLUS
Anon	1996			WO 9622976	CAPLUS
Anon	1996			WO 9640116	CAPLUS
Anon	1998			WO 9807695	CAPLUS
Anon	1998			WO 9807835	CAPLUS
Anon	1998			WO 9845708	CAPLUS
Anon	1998			WO 9850356	CAPLUS
Anon	1998			WO 9856376	CAPLUS
Anon	1999			WO 9910325	CAPLUS
Anon	1999			WO 9910325	CAPLUS
Arteaga	1983	84	1418	J Clin Invest	
Arteaga	1989	84	1418	J Clin Invest	CAPLUS
Arvidsson	1994	14	6715	Molecular and Cellul	CAPLUS
Baserga	1995	55	249	Cancer Research	CAPLUS
Baserga	1995	55	249	Cancer Research	CAPLUS
Baserga	1994	79	927	Cell	CAPLUS
Beilstein				Beilstein Reg No 252	
Beilstein	1923	56		Beilstein Reg No 252	
Bolen	1992	6	3403	FASEB J	CAPLUS
Bolen	1992	6	3403	FASEB J	CAPLUS
Bolen	1993	8	2025	Oncogene	CAPLUS
Bolen	1993	8	2025	Onogene	CAPLUS
Bonner	1985	5	1400	Molecular and Cellul	CAPLUS
Bonner	1985	5	1400	Molecular and Cellul	CAPLUS
Buzzetti	1995			US 5397787 A	CAPLUS
Buzzetti	1998			US 5840745 A	CAPLUS
Buzzetti	1993	48	615	II Farmaco	CAPLUS
Cance	1993	54	571	Int J Cancer	CAPLUS
Cance	1993	54	571	Int J Cancer	CAPLUS
Carpenedo	1977	244	74	Analytical Biochemis	
Carpenedo	1997	244	74	Analytical Biochemis	CAPLUS
Chen	1977			Chinese Journal of P	
Chen	1997	40	149	Chinese Journal of P	CAPLUS
Claesso-Welsh	1994	5	37	Progress in Growth F	
Coppola	1994	14	4558	Molecular and Cellul	

Coppola	1994	14	4588	Molecular and Cellul	CAPLUS
Damiani	1994	48	1155	Biochemical Pharmaco	CAPLUS
Damiani	1994	48	1155	Biochemical Pharmaco	CAPLUS
Davis	1973	16	1043	Journal of Medicinal	CAPLUS
Davis	1975	16	1043	Journal of Medicinal	
de Vires	1992	255	989.	Science	
Decker	1988	15	61	J Immunol Methods	
Decker	1988	15	61	J Immunol Methods	
Dickson	1992	61	249	Cancer Treatment Res	CAPLUS
Dickson	1992	61	249	Cancer treatment Res	CAPLUS
Eissenstat	1994			US 5330992 A	CAPLUS
Fantl	1992	69	413	Cell	CAPLUS
Fantl	1992	69	413	Cell	CAPLUS
Fendly	1990	50	1550	Cancer Research	CAPLUS
Fendly	1990	50	1550	Cancer Research	CAPLUS
Ferrara	1989	161	851	Biochemical and Biop	CAPLUS
Fingl	1975		1	The Pharmacologial B	CAPLUS
Fingl	1975		1	The Pharmacological	CAPLUS
Floege	1993	43	369	Kidney International	CAPLUS
Floege	1993	43	S47	Kidney International	CAPLUS
Floege	1993	43	S47	Kidney International	CAPLUS
Folkman	1987		583	Congress of Thrombos	
Folkman	1992	267	10931	J Bio Chem	CAPLUS
Folkman	1990	82	4	Journal fo National	MEDLINE
Folkman	1971	285	1182	New England J Medici	MEDLINE
Gazit	1991	34	1896	J Med Chem	CAPLUS
Gennaro	1990			Remington's P; harma	
Goldring	1991	1	301	Critical Reviews in	CAPLUS
Goldring	1991	1	301	Critical Reviews in	CAPLUS
Graziani	1993	268	9165	The Journal of Biolo	CAPLUS
Graziani	1993	268	9165	The Journal of Biolo	CAPLUS
Honegger	1987	51	199	Cell	CAPLUS
Honegger	1987	51	199	Cell	CAPLUS
Houben-Weyl	1999	E231	834	Cyclic Compounds V B	
Houck	1992	267	26031	J Bio Chem	CAPLUS
Hu	1992	12	981	Molecular and Cellul	CAPLUS
Jellinek	1994	33	10450	Biochemistry	CAPLUS
Jellinek	1994	33	10450	Biochemistry	CAPLUS
Kashishian	1993	4	49	Molecular Biology of	CAPLUS
Kashishian	1992	11	1373	The Embo Journal	CAPLUS
Kato	1993	616	67	Journal of Chromatog	CAPLUS
Kato	1993	616	67	Journal of Chromatog	CAPLUS
Kazlauskas	1993	90	6939	Proc Natl Acad Sci U	CAPLUS
Kendall	1993	90	10705	Proc Natl Acad Sci U	CAPLUS
Kendall	1993	90	10705	Proc Natl Acad Sci U	CAPLUS
Kim	1993	362	841	Nature	CAPLUS
Kim	1993	362	841	Nature	CAPLUS
Kinsella	1992	199	56	Exp Cell Research	CAPLUS
Kinsella	1992	199	56	Exp Cell Research	CAPLUS
Klagsburn	1993	3	699	Current Biology	
Koch	1991	252	668	Science	CAPLUS
Koch	1991	252	668	Science	CAPLUS
Komada	1993	8	2381	Oncogene	CAPLUS
Komada	1993	8	2381	Oncogene	CAPLUS
Korc	1992	90	1352	J Clin Invest	MEDLINE
Korc	1992	90	1352	J Clin, Invest	MEDLINE
Korzeniewski	1983	64	313	J Immunol Methods	CAPLUS
Kumabe	1992	7	627	Oncogene	CAPLUS
Kumabe	1992	7	627	Oncogene	CAPLUS
Lee	1992	118	1057	Journal of Cell Biol	CAPLUS
Lee	1992	118	1057	Journal of Cell Biol	CAPLUS
Levitzki	1993			US 5196446 A	CAPLUS
Levitzki	1993			US 5217999 A	CAPLUS

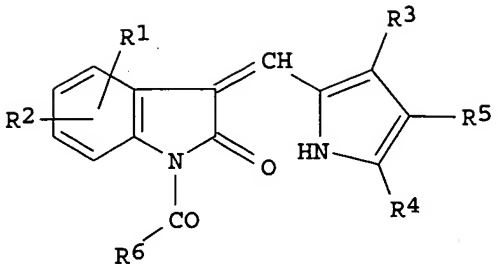
Levitzki	1992	267	633	Science	
Maass	1993	37	2612	Antimicrobial Agents	CAPLUS
Maass	1993	37	2612	Antimocrobial Agents	CAPLUS
Macauley	1990	50	2511	Cancer Research	
Macauley	1990	50	2511	Cancer Research	
Mariani	1994			Experimental Therape	
Mariani	1994			Experimental Therape	
Millauer	1993	72	835	Cell	CAPLUS
Mohammad	1997	276	955	Science	
Moreto	1979	29	1561	Arzneimittel-Forschu	
Moreto	1979	29	1561	Arzneimitttel-Forsch	
Moreto	1976	36	221	European Journal of	CAPLUS
Moreto	1976	36	221	European Journal of	CAPLUS
Morrison	1988	85	8855	Proc Natl Acad Sci U	CAPLUS
Morrison	1988	85	8855	Proc Natl Acad Sci U	CAPLUS
Mosmann	1983	65	55	J Immunol Methods	MEDLINE
Mosmann	1983	65	55	J Immunol Methods	MEDLINE
Nishimura	1993	13	6889	Molecular and Cellul	CAPLUS
Plowman	1994	7	334	DN & P	
Plowman	1994	7	334	DN&P	
Quinn	1993	90	7533	Proc Natl Acad Sci U	CAPLUS
Rovnyak	1977			US 4002749 A	CAPLUS
Rovnyak	1977			US 4053613 A	CAPLUS
Rozakis-Adcock	1992	360	689	Nature	CAPLUS
Rygaard	1969	77	758	Acta path Microbiol	MEDLINE
Rygaard	1969	77	758	Acta path microbiol	MEDLINE
Sandberg-Nordqvist	1993	53	2475	Cancer Research	CAPLUS
Sandberg-Nordqvist	1993	53	3475	Cancer Research	
Schlessinger	1992	9	383	Neuron	CAPLUS
Schlessinger	1992	9	383	Neuron	CAPLUS
Shibuya	1990	5	519	Oncogene	CAPLUS
Shiraishi	1987	147	322	Biochemical and Biop	CAPLUS
Singh	1990	5	519	Bollettino Chimico F	
Singh	1994	133	76	Bollettino Chimico F	CAPLUS
Singh	1989	144	105	Zentralbl Mikrobiol	CAPLUS
Singh	1989	144	105	Zentralbl, Mikrobiol	CAPLUS
Sinkula, A	1975	10	306	Annual Reports in Me	CAPLUS
Sircar	1994			US 5322950 A	CAPLUS
Slamon	1989	244	707	Science	MEDLINE
Slamon	1989	244	707	Science	MEDLINE
Soldi	1996	13	515	Oncogene	CAPLUS
Songyang	1993	72	767	Cell	CAPLUS
Songyang	1993	72	767	Cell	CAPLUS
Songyang	1994	14	2777	Molecular and Cellul	CAPLUS
Songyang	1994	14	2777	Molecular and Cellul	CAPLUS
Spada	1994			US 5302606 A	CAPLUS
Spada	1999			US 36256 E	CAPLUS
Spada	1995	5	805	Expert Opinion on Th	CAPLUS
Sun	1998	41	2588	J Med Chem	CAPLUS
Superti-Furga	1993	12	2625	EMBO J	CAPLUS
Superti-Furga	1993	12	2625	Embo J	CAPLUS
Superti-Furga	1996	14	600	Nature Biotech	CAPLUS
Superti-Furga	1996	14	600	Nature Biotech	CAPLUS
Takano	1993	4	358A	Mol Bio Cell, abstra	
Takano	1993	4	358A	Mol Bio Cell, abstra	
Tang	1998			US 5786488 A	CAPLUS
Tang	1998			US 5792783 A	CAPLUS
Tang	1999			US 5880141 A	CAPLUS
Tang	1999			US 5883113 A	CAPLUS
Tang	1999			US 5883116 A	CAPLUS
Tang	1999			US 5886020 A	CAPLUS
Torp	1992	100	713	AMPIS	MEDLINE
Torp	1992	100	713	AMPIS	MEDLINE

Traxler	1977	7	571	Expert Opinion on Th	
Trost	1991	4	478	Selectivity, Strateg	
Tsai	1992	31	943	Neuorpharmacology	CAPLUS
Tsai	1992	31	943	Neuropharmacology	CAPLUS
Tuzi	1991	63	227	Br J Cancer	MEDLINE
Tuzi	1991	63	227.	Br J Cancer	MEDLINE
Twamley-Stein	1993	90	7696	Proc Natl Acad Sci	CAPLUS
Vaisman	1990	265	19461	J Biol Chem	CAPLUS
Vallee	1990			US 4966849 A	CAPLUS
Varma	1989	66	804	J Indian Chem Soc	CAPLUS
Voller	1980		359	Manual of Clinical I	
Voller	1980		359	Manual of Clinical I	
Voller	1980		359	Manual of Clinical I	
Walker	1965	8	626	J Med Chem	CAPLUS
Weidner	1991	324	1	New England Journal	MEDLINE
Wright	1992	152	448	J Cellular Physiolog	CAPLUS
Wright	1992	152	448	J Cellular Physiolog	CAPLUS
Wright	1992	152	448	J Cellular Physiolog	CAPLUS
Zaman	1999	57	57	Biochemical Pharmaco	CAPLUS
Zaman	1999	57	57	Biochemical Pharmaco	CAPLUS
Zhang	1996	49	228	Molecular Pharmacolo	
Zhang	1996	49	228	Molecular Pharmacolo	

L31 ANSWER 2 OF 4 MARPAT COPYRIGHT 2005 ACS on STN
AN 137:294870 MARPAT
TI Preparation of prodrugs of 3-(pyrrol-2-ylmethylidene)-2-indolinones and activity as modulators of protein kinases
IN Sun, Connie Li; Wei, Chung Chen; Tang, Peng Cho; Koenig, Marcel; Zhou, Yong; Vojkovsky, Tomas; Nematalla, Asaad S.
PA Sugen, Inc., USA
SO PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002081466	A1	20021017	WO 2002-US11001	20020409
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003100555	A1	20030529	US 2002-118321	20020409
	US 6797725	B2	20040928		
	US 2004186161	A1	20040923	US 2004-816957	20040405
PRAI	US 2001-282630P		20010409		
	US 2002-118321		20020409		

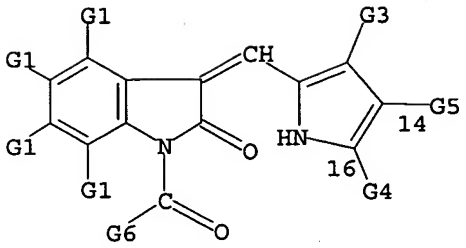
GI



I

AB The present invention relates to pyrrole substituted 2-indolinone compds. (shown as I; e.g. 3-[1-(3,5-dimethyl-1H-pyrrol-2-yl)meth-(Z)-ylidene]-2-oxo-2,3-dihydroindole-1-carbonyl chloride) and their pharmaceutically acceptable salts which modulate the activity of protein kinases and therefore are expected to be useful in the prevention and treatment of protein kinase related cellular disorders such as cancer (no data). In I, R1 and R2 are independently H, halo, alkyl, alkylthio, nitro, trihalomethyl, hydroxy, hydroxyalkyl, alkoxy, cyano, aryl, heteroaryl, -C(O)R7 (R7 is alkyl, amino, hydroxy, alkoxy, aryl, heteroaryl, aryloxy, heteroaryloxy, heterocycle, and aminoalkylamino), -NR8R9, -NR8C(O)R9, -SO2R8, and -S(O)2NR8R9 (R8 and R9 are independently H, alkyl, aryl and heteroaryl, or R8 and R9 together with the N to which they are attached form a saturated heterocycloamino). R3 is H, alkyl, hydroxyalkyl, aminoalkyl, -C(O)R7, aryl, and heteroaryl; R4 is H, alkyl, -C(O)R7 aryl, and heteroaryl. R5 is H and -COR10 where R10 is alkyl, alkoxy, hydroxy, aryl, aryloxy, heteroaryl, heterocycle, alkylamino, dialkylamino, or -NR11R12 where R11 is H or alkyl, and R12 is aminoalkyl, hydroxyalkyl, acetylalkyl, cyanoalkyl, carboxyalkyl, alkoxycarbonylalkyl, heteroaralkyl, or heterocyclylalkyl wherein the alkyl chain in aminoalkyl, heteroaralkyl, heteroaralkyl, or heterocyclylalkyl is optionally substituted with one or two hydroxy group(s); or R4 and R5 together form - (CH2)4- or -(CH2)mCO(CH2)n- wherein n is 0 to 3, provided that n+m is 3. R6 is: (c) -OR13 wherein R13 is alkyl, trifluoromethyl, carboxyalkyl, aminoalkyl, phosphonooxyalkyl, sulfooxyalkyl, hydroxyalkyl, alkoxyalkyl, aryl, heteroaryl, heteroaralkyl, heterocyclyl, monosaccharides and heterocyclylalkyl wherein the alkyl chain in carboxyalkyl, aminoalkyl, phosphonooxyalkyl, sulfooxyalkyl, heteroaralkyl, heterocyclylalkyl, hydroxyalkyl, or alkoxyalkyl is optionally substituted with one or two hydroxy group(s) and further wherein one or two C atoms in said alkyl chain are optionally replaced by O, -NR14- (R14 is H or alkyl), -S-, or -SO2-; or. (d) -NR15R16 where are R15 and R16 are independently H, alkyl, carboxyalkyl, alkoxyalkyl, aminoalkyl, phosphonooxyalkyl, sulfooxyalkyl, hydroxyalkyl, aryl, heteroaryl, heteroaralkyl, and heterocyclylalkyl; wherein the alkyl chain in carboxyalkyl, aminoalkyl, phosphonooxyalkyl, heteroaralkyl, heterocyclylalkyl, hydroxyalkyl, or alkoxyalkyl is optionally substituted with one or two hydroxy group(s) and further wherein one or two C atoms in the alkyl chain are optionally replaced by O, -NR17- (R17 is H or alkyl), -S-, or -SO2-; or R15 and R16 together with the N atom to which they are attached form saturated or unsatd. heterocycloamino;. Although the methods of preparation are not claimed, >80 example prepns. are included, both of I and the unprotected version of I in which the C(O)R6 group has been replaced by H.

MSTR 1



G5 = 55

C(O)-G10
55

G6 = 70

O——G13
70

G10 = alkylamino<(1-20)>
MPL: claim 1
NTE: or pharmaceutically acceptable salts
NTE: additional heteroatom interruptions also claimed
NTE: additional oxo substitution also claimed

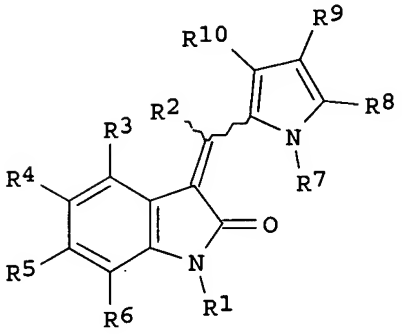
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Anthony, M	2000			WO 0008202 A	CAPLUS
Sugen Inc	1999			WO 9961422 A	CAPLUS
Wilson, M	2001			WO 0190103 A	CAPLUS

L31 ANSWER 3 OF 4 MARPAT COPYRIGHT 2005 ACS on STN
AN 135:19549 MARPAT
TI Preparation of pyrrole substituted 2-indolinones as antitumor agents
IN Shenoy, Narmada; Sorasuchart, Waranush
PA Sugen, Inc., USA
SO PCT Int. Appl., 249 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001037820	A2	20010531	WO 2000-US32277	20001122
	WO 2001037820	A3	20011213		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1233943	A2	20020828	EP 2000-982228	20001122
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

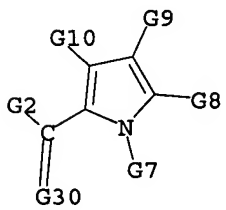
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2003514851 T2 20030422 JP 2001-539435 20001122
PRAI US 1999-167544P 19991124
WO 2000-US32277 20001122
GI



I

AB The title compds. [I; R1 = H, alkyl, alkenyl, etc.; R2 = H, halo, alkyl, etc.; R3-R6 = H, alkyl, trihaloalkyl, etc.; R3 and R4, R4 and R5, R5 and R6 may combine to form a six membered aryl ring, OCH2O, OCH2CH2O; R7 = H, alkyl, cycloalkyl, etc.; R8-R10 = H, alkyl, trihaloalkyl, etc.] were prepared and formulated. E.g., a multi-step synthesis of I [R1-R7 = H; R8, R10 = Me; R9 = (CH2)2CO2H] which showed 79-86% inhibition of tumor growth of Calu-6 cells in mice at 75 and 100 mg/kg/day, was given. The present invention features formulations of indolinones which compds. are ionizable as free acids or free bases. The formulation is suitable for parenteral or oral administration, wherein the formulation comprises an ionizable substituted indolinone, and a pharmaceutically acceptable carrier therefor. The term "ionizable substituted indolinone" includes pyrrole substituted 2-indolinones I which, in addition to being otherwise optionally substituted on both the pyrrole and 2-indolinone portions of the compound, are necessarily substituted on the pyrrole moiety with one or more hydrocarbon chains which themselves are substituted with at least one polar group.

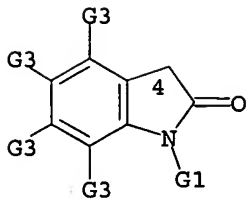
MSTR 1



G1 = CO2H
G9 = 299

C(O)-G17
299

G17 = NH2
G30 = 4

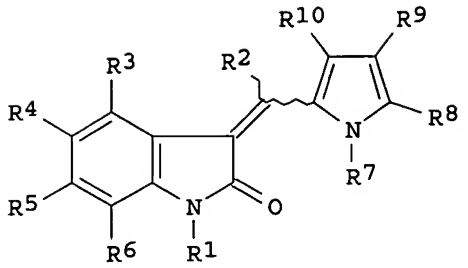


MPL: claim 2
NTE: oxo substitution in alkyl group is also claimed
NTE: substitution is restricted
NTE: additional ring formation also claimed

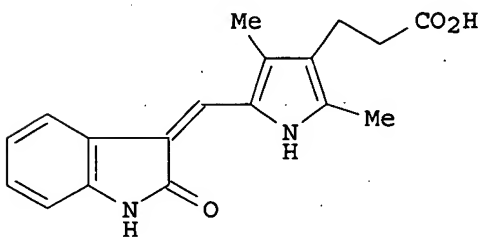
L31 ANSWER 4 OF 4 MARPAT COPYRIGHT 2005 ACS on STN
AN 132:12257 MARPAT
TI Preparation of pyrrole substituted 2-indolinone protein kinase inhibitors
IN Tang, Peng Cho; Sun, Li; McMahon, Gerald
PA Sugen, Inc., USA
SO PCT Int. Appl., 240 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9961422	A1	19991202	WO 1999-US12069	19990528
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2314156	AA	19991202	CA 1999-2314156	19990528
	AU 9944102	A1	19991213	AU 1999-44102	19990528
	AU 759226	B2	20030410		
	EP 1082305	A1	20010314	EP 1999-927120	19990528
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9910792	A	20020129	BR 1999-10792	19990528
	TR 200003514	T2	20020521	TR 2000-20000351	19990528
	US 6395734	B1	20020528	US 1999-322297	19990528
	JP ~~2002516310~~	T2	20020604	JP 2000-550828	19990528
	NO 2000005916	A	20010129	NO 2000-5916	20001122
	US 2003105151	A1	20030605	US 2002-81147	20020225
PRAI	US 1998-87310P	19980529			
	US 1999-116106P	19990115			
	US 1999-322297	19990528			
	WO 1999-US12069	19990528			

GI



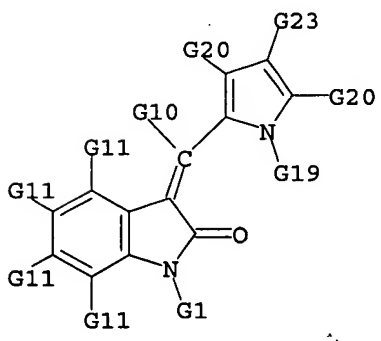
I



II

AB The present invention relates to 5-(2-oxo-1,2-dihydroindol-3-ylidenemethyl)-1H-pyrrol-3-ylalkanoic acid derivs. (I) [where R1 and R7 = independently H, (cyclo)alkyl, alkenyl, alkynyl, aryl, OH, alkoxy, carboxy, acetyl, (thio)amido, (trihalomethane)sulfonyl, etc.; R2 = H, halo, (cyclo)alkyl, (hetero)aryl, or heteroalicyclic; R3, R4, R5, R6, R8, R9, R10 = independently H, (cyclo)alkyl, trihaloalkyl, alkenyl, alkynyl, (hetero)aryl(oxy), heteroalicyclic, OH, alkoxy, SH, alkylthio, arylthio, sulfinyl, sulfonyl, sulfonamido , carbonyl, carboxy, amido, CN, NO2, halo, (thio)carbamyl, (un)substituted amino, etc.] which modulate the activity of protein kinases and are useful in the prevention and treatment of protein kinase related cellular disorders, such as cancer. Thus, 2,4-dimethyl-5-ethoxycarbonyl-3-(2-ethoxycarbonylethyl)pyrrole was deprotected using NaOH to form 3-(2-carboxyethyl)-2,4-dimethylpyrrole (100%) and the product C-5 formylated (two methods given for 86% and 90% yield, resp.). Reaction with 2-oxindole in EtOH and pyrrolidine or in aqueous NaOH yielded II (88% and 91%, resp.), which reduced the average size of C6 human glioma and melanoma tumors s.c. implanted in mice by 80-85%. II, when administered orally, demonstrated notably superior efficacy compared to structurally similar analogs.

MSTR 1



G1 = 19

```
C(O)-G2
19


G2      = OH
G6      = NH2
G23     = 201


C(O)-G6
201


MPL:      claim 1
NTE:      substitution is restricted
```

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Mohammadi	1998			WO 980783526	CAPLUS
Mohammadi	1997	276	955	Science	CAPLUS
Sun		41	2588	J Med Chem	CAPLUS
Tang	1996			WO 9640116	CAPLUS
Tang	1998			WO 9807695	CAPLUS

```
=> d his

     (FILE 'HOME' ENTERED AT 10:14:02 ON 15 JAN 2005)
                SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 10:14:15 ON 15 JAN 2005
L1             1 S (US20040186161 OR US6797725 OR US20030100555)/PN OR (US2001-2
                 E SUN C/AU
L2           159 S E3,E18
                 E SUN CONNIE/AU
L3             4 S E4
                 E WEI C/AU
L4           137 S E3,E5
                 E WEI CHUNG/AU
L5            42 S E5
                 E TANG P/AU
L6            36 S E3,E4
                 E TANG PENG/AU
L7            99 S E3-E5
                 E KOENIG M/AU
L8           234 S E3-E15,E17,E18
                 E ZHOU Y/AU
L9          1375 S E3-E24
                 E ZHOU YONG/AU
L10         1287 S ZHOU YONG?/AU
                 E VOJKOVSK/AU
L11           12 S E5,E6
                 E NAMATALLA A/AU
                 E NEMATALLA/AU
L12           18 S E4-E6
                 E SUGEN/PA,CS
L13          260 S E3-E27
                 SEL RN L1

     FILE 'REGISTRY' ENTERED AT 10:18:05 ON 15 JAN 2005
L14          255 S E1-E255
L15               STR
```

```
L16             0 S L15
L17           139 S L14 AND NC4-C6/ES AND NR>=3
L18           124 S L17 AND NC4/ES
L19            87 S L18 AND N>=3
L20               STR L15
L21            50 S L20
L22          2680 S L20 FUL
                  SAV L22 SHIAO816/A
L23               STR L15
L24             3 S L23 SAM SUB=L22
L25            48 S L23 FUL SUB=L22
                  SAV L25 SHIAO816A/A
L26               STR L15
L27             0 S L26 SAM SUB=L25
L28             0 S L26 FUL SUB=L25
                  SAV L28 SHIAO816B/A

     FILE 'REGISTRY' ENTERED AT 10:28:16 ON 15 JAN 2005

     FILE 'MARPAT' ENTERED AT 10:28:29 ON 15 JAN 2005
L29             0 S L28 SAM
L30             8 S L28 FUL
                  SAV L30 SHIAO816C/A
L31             4 S L15 FUL SUB=L30
                  SAV L31 SHIAO816D/A

     FILE 'MARPAT' ENTERED AT 10:31:10 ON 15 JAN 2005

=>
```